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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/929,665	BANDER, NEIL H.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *144,156-168 and 170-210* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *144,156-168 and 170-210* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20070205*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed February 2, 2007, is acknowledged and has been entered. Claims 144, 159, 172, 178, 180, 184-187, 192-195, 200-203, 206, 207, 209, and 210 have been amended.

2. Claims 144, 156-168, and 170-210 are pending in the application and are currently under prosecution.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following Office action contains NEW GROUNDS of rejection.

Information Disclosure Statement

5. The information disclosure filed February 2, 2007, has been considered. An initialed copy is enclosed.

Terminal Disclaimers

6. The terminal disclaimers filed on February 2, 2007, disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration dates of U.S. Patent No. 6,649,163, U.S. Patent No. 7,045,605, or any patent granted on Application No. 10/379,838, have been reviewed and are accepted. The terminal disclaimers have been recorded.

Ownership

7. As noted in the preceding Office action, claims 144, 156-168, 170-178, and 180-210 are directed to an invention not patentably distinct from claims 1-142 of commonly assigned U.S. Patent No. 7,045,605 B2. Specifically, although the conflicting claims are

not identical, they are not patentably distinct from each other for the reasons set forth in the preceding Office action.

The rejection on the ground of nonstatutory obviousness-type double patenting has been rendered moot by the terminal disclaimer filed February 2, 2007.

Nevertheless, the issue remains as to the inventions were commonly owned *at the time the invention in this application was made*, so as to preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Again, the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 7,045,605 B2, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

8. As further noted in the preceding Office action, claims 144, 156-168, 170-177, 180, 184-203, and 208-210 are directed to an invention not patentably distinct from claims 1-142 of commonly assigned copending Application No. 10/379,838. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth in the preceding Office action.

The rejection on the ground of nonstatutory obviousness-type double patenting has been rendered moot by the terminal disclaimer filed February 2, 2007.

Nevertheless, the issue remains as to the inventions were commonly owned *at the time the invention in this application was made*, so as to preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Again, the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned copending Application No. 10/379,838, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Grounds of Objection and Rejection Withdrawn

9. Unless specifically reiterated below, Applicant's amendment and/or arguments filed February 2, 2007, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed August 4, 2006.

Priority

10. Applicant's claim under 35 U.S.C. § 120 for benefit of the earlier filing date of the U.S. Patent Application No. 09/357,704, filed July 20, 1999, which claims benefit of U.S. Patent Application No. 08/838,682, filed April 9, 1997, which claims benefit of U.S. Provisional Application No. 60/022,125, filed July 18, 1996, and U.S. Provisional Application No. 60/016,976, filed May 6, 1996, is acknowledged.

However, claims 144, 156-168, and 170-210 do not properly benefit under 35 U.S.C. § 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and/or a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under 35 U.S.C. § 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Accordingly, the effective filing date of claims 144, 156-168, and 170-210 is deemed the filing date of the instant application, namely August 13, 2001.

Ground of Objection Maintained

11. The objection to the specification for the following reason is maintained:

At page 1, paragraph 1, of the specification there is a statement that this application is a continuation application of Application Serial No. 09/357,704, which is a divisional of Application Serial No. 08/836,682. The latter of these prior filed applications has since issued as U.S. Patent No. 6,107,090; yet the specification does not properly indicate the status of this application.

Appropriate correction is required.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 144, 156-168, and 170-210 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 144, 156-168, and 170-210 are directed to a genus of antibodies or antigen-binding fragments thereof, which compete for binding to prostate specific membrane antigen (PSMA) with a monoclonal antibody selected from the group consisting of E99, J415, J533 and J591 monoclonal antibody produced by hybridomas deposited under ATCC accession numbers HB-12101, HB-12109, HB12127, and HB-12126, respectively.

The claims are indefinite for the following reasons:

The claims are indefinite because of the recitation in claim 144, for example, of "which competes for binding to prostate specific membrane antigen (PSMA) with a monoclonal antibody" selected from the specified group of monoclonal antibodies.

At paragraph [0079], for example, of the published application[1], the specification discloses: "Whether two biological agents bind to competing or non-competing binding sites can be determined by conventional competitive binding assays". The specification describes the binding assay, which was used to determine, allegedly, whether monoclonal antibodies J591, J533, E99, and J415 detect the same or different epitopes; see, e.g., paragraphs [0104]-[0106] of the published application. As explained in paragraph [0105], the controls used as the basis for this determination consisted of using the same monoclonal antibody both cold and labeled to define "100% competition", or using monoclonal antibody to a totally different molecule (e.g., monoclonal antibody I-56, which detects inhibin) to define "0% competition". Thus, according to these disclosures, it is evident that one determines whether an antibody

"competes" for binding to PSMA with one of the selected antibodies by measuring the percentage of binding of a detectably labeled antibody in the presence of an unlabeled (i.e., "cold") antibody.

Nevertheless, it is aptly noted that the term "competes" is not expressly defined in the specification, so it may not be immediately clear what functional attribute characterizes the claimed antibody or antigen binding fragment thereof; moreover, as discussed in greater detail below, the degree to which the claimed antibody "competes" for binding to PSMA with any one of the recited monoclonal antibodies, nor the methodology used to make the determination, and the conditions under which that determination are made, are not delineated by the claims and are not ascertainable from the disclosure.

The term "competition" is defined, for example, by Stedman's Online Medical Dictionary, 27th Edition as meaning: "The process by which the activity or presence of one substance interferes with, or suppresses, the activity of another substance with similar affinities" (Copyright © 2006 Lippincott Williams & Wilkins). Given this definition, the claims are directed to antibodies or antigen-binding fragments thereof that interfere with, or suppress binding of one of the selected monoclonal antibodies to PSMA, as perhaps determined using the exemplified binding assay.

This interpretation is not inconsistent with the specification, which at paragraph [0106], for example, discloses: "The results indicated that J591, J533, and E99 each **interfere, compete, or block** binding of one another but do not block binding of J415 and vice versa" (emboldened for emphasis).

Thus, while one may know how to determine whether an antibody "competes" with one of the selected monoclonal antibodies, it is apparent that the degree to which an antibody competes with another antibody is a relative or subjective expression, and the requisite degree to which the claimed antibody competes with any of the selected monoclonal antibodies cannot be ascertained from the disclosure.

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[1] U.S. Patent Application Publication No. 2003/0003101 A1.

Contrary to the assertion in the specification that such a binding assay determines whether two antibodies bind to the same antigenic determinant (i.e., epitope), competing antibodies do not necessarily bind the same epitopes. For example, "competing" antibodies may bind spatially overlapping but discrete epitopes. Simply because two antibodies cannot simultaneously occupy the same space, such an antibody, once bound to the antigen, sterically hinders or blocks binding of another such antibody. As another example, a "competing" antibody might not necessarily bind to the same epitope of an antigen as another antibody, if one of the antibodies induces conformational shifts in the three-dimensional structure of the antigen upon binding, which prevents binding of the other antibody to the antigen because the epitope to which it would otherwise bind is unrecognizable as a consequence of the structural change.

In addition, it is recognized that the degree of binding of an antibody, which is observed in the exemplified competitive binding assay, will depend upon the concentration of the detectably labeled antibody and the unlabeled competing antibody. Typically, the higher the concentration of the unlabeled competitor, the lower the percentage of binding of the labeled antibody. So, at *high enough* concentrations, any antibody might be deemed capable of "competing" for binding to an antigen with any other antibody, regardless of whether or not the different antibodies bind to the same, or even overlapping epitopes.

George et al. (*Circulation*. 1998; **97**: 900-906), for example, describes different antibodies, which do not bind to the same epitope of an antigen, but are nevertheless capable of competing with one another for binding to the antigen; see entire document (e.g., page 903, paragraph bridging columns 1 and 2). More particularly, George et al. describes three antibodies, which bind decidedly different, non-cross-reactive epitopes on β2GPI; yet, George et al. teaches each is able to "compete" *to some extent* with any of the others for binding to the antigen (page 903, paragraph bridging columns 1 and 2). For example, George et al. teaches monoclonal antibody ILA-4 competed with itself for binding to the antigen (% inhibition = 90 ± 11% at competitor antibody concentrations of

30 μg/ml), but George et al. discloses, despite its binding a non-overlapping epitope, monoclonal antibody ILA-1 also "competed", albeit perhaps unsubstantially with monoclonal antibody ILA-4 for binding to the antigen (% inhibition = 9 ± 4%).

Accordingly, George et al. illustrates the capricious and arbitrary nature of determinations that different antibodies bind to the same or different epitopes, which are based upon the results of competitive binding assays, such as the assay exemplified in the specification. Although each of the described antibodies "competed" to a measurable extent with the other antibodies for binding to the antigen, George et al. nevertheless concludes "no competition was achieved", and the antibodies bind distinct, non-overlapping epitopes.

Therefore, the claims are *not* unambiguously interpreted, as it cannot be determined whether the antibody to which the claims are directed is an antibody that merely inhibits, but does not abrogate the interaction between the selected antibody and PSMA. Moreover, if the claimed antibody merely inhibits binding of the selected antibody to PSMA, it cannot be determined to what requisite extent the claimed antibody must "compete" for binding to PSMA with the selected antibody.

Finally, the claims are directed to a plurality of monoclonal antibodies that are produced by any of the recited deposited hybridomas. Pointedly, different members of this plurality of antibodies do not necessarily bind PSMA with the same affinity or avidity as any of the other monoclonal antibodies produced by another of the deposited hybridomas. For example, monoclonal antibody J591, which is produced by the hybridoma deposited under ATCC accession number HB-12126, may have a substantially different binding affinity than monoclonal antibody E99, which is produced the hybridoma deposited under ATCC accession number HB-12101. Presuming the concentration of the antibody is not altered, depending upon the affinity and avidity that characterizes any given antibody's ability to bind an antigen, the antibody is expected to more or less effectively "compete" with another antibody that binds the same antigen. Accordingly, the metes and bounds of the subject matter that is encompassed by the claims is expected to vary depending upon which of the recited antibodies is selected

and the conditions under which the ability of the claimed antibody to compete is determined.

Summarizing these points, then, it is submitted that the metes and bounds of the subject matter encompassed by the claims vary, depending upon one's interpretation of the language of those claims, as well as upon the binding characteristics of the antibody that is selected from any of the recited pluralities of monoclonal antibodies; and while notably claims could and should be given the broadest, reasonable interpretation, the claims fail to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, as they do not delineate the claimed subject matter with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing subject matter.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 178, 179, 181-183, 204, 206, and 207 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

(a) Claims 178 and 179 are directed to a genus of "cells" that produces an antibody that competes for binding to PSMA with a selected monoclonal antibody. Claim 179 is more particularly directed to members of this genus of such cells, which are derived from a lymphocytic cell line.

Claims 178 and 179 were added by the amendment filed March 22, 2002. At page 8 of that amendment Applicant has asserted that support for these claims is found in the specification, as filed, in the originally filed claims, as well as in the disclosure,

e.g., at page 16, line 16, through page 17, line 4; page 25, lines 16-35; page 35, Table 3); page 19, lines 20-36 and Table 1; page 11, lines 21-33; page 37, line 24, through page 39, line 14; page 18, line 33, through page 19, line 7; page 40, line 14, through page 45, line 14; page 20, line 1, through page 29, line 10; page 21, lines 19-30; and page 6, lines 5-22.

Contrary to Applicant's assertions, none of originally filed claims nor any of the particular disclosures describes a genus of cells, including such cells derived from a lymphocytic cell line, which produce an antibody that competes for binding to PSMA with a selected monoclonal antibody.

Originally filed claims 64-67 (now canceled) were drawn to a genus of hybridomas that produce an antibody that binds the extracellular domain of PSMA, including the deposited hybridomas that produced monoclonal antibodies E99, J415, J533, and J591; but none of the originally filed claims describes such antibodies that compete for binding to PSMA with any of the monoclonal antibodies produced by these hybridomas, and none of the originally filed claims describes a subgenus of such cells, which are derived from a lymphocytic cell line.

Similarly, the originally filed disclosure describes these same hybridomas, but does not describe with any degree of particularity a genus of "cells" that produce an antibody that competes for binding to PSMA with any of the monoclonal antibodies produced by those hybridomas. For example, at paragraph [0033] of the published application, the specification describes hybridoma cell lines, which produce monoclonal antibodies that recognize an extracellular domain of PSMA, bind PSMA and/or are internalized with PSMA. Then, at paragraph [0054] of the published application, the specification discloses production of such monoclonal antibodies may be effected by techniques, which are well-known in the art and basically involve: (a) obtaining immune cells (i.e., lymphocytes) from the spleen of a mammal (e.g., mouse) that has been previously immunized with the antigen of interest, and (b) fusing the antibody-secreting lymphocytes with mouse myeloma cells or other transformed cells, which are capable of replicating indefinitely in cell culture, so as to produce immortal, immunoglobulin-secreting cell lines, or hybridomas, which are then cultured and screened for the

production of the desired monoclonal antibodies. None of these disclosures, however, describes with any degree of particularity the genus of "cells" to which the claims are directed, as none describes the type and nature of the cells, apart from hybridomas, producing such antibodies, and especially not such cells that are derived from a lymphocytic cell line, per se.

Consequently, the addition of 178 and 179 appears to have introduced new matter, thereby violating the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

This issue might be remedied if Applicant were to point to particular disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary support for the language of the present claims.

(b) Claims 181-183, 204, 206, and 207 are directed to a kit for detecting any of a genus of "cancers". Claim 204 is more particularly directed to the kit of claim 181, wherein the cancer is selected from the group consisting of any of several specifically recited types of cancer (e.g., lung cancer).

Claims 181-183 were amended and claims 206 and 207 were added by the amendment filed December 1, 2003. At page 13 of that amendment Applicant has asserted support for the amendments can be found in the specification at, for example, page 27, lines 26-35; page 28, lines 6-10; and page 38, lines 11-21.

Contrary to Applicant's assertion, it does not appear the specification, including the claims, as originally filed, provides the necessary support for the language of claims drawn to kits for detecting any of a genus of different types of cancer, with the notable exception of a kit for detecting prostate cancer.

Originally filed claims 59-63 (now canceled) were directed to a kit for detecting prostate cancer; none of the originally filed claims describes kits for detecting any other type of cancer, such as, for example, lung cancer.

Similarly, while at paragraph [0052] of the published application, for example, the specification describes methods of detecting normal, benign hyperplastic, and cancerous prostate epithelial cells, which certainly provides implicit support for claims directed to kits for performing such methods, the specification does not describe with

any particularity other types of cancer that are detected using any of the disclosed products or methods for using those products.

Consequently, the amendment to claims 181-183 and the addition of 204, 206, and 207 appears to have introduced new matter, thereby violating the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

This issue might be remedied if Applicant were to point to particular disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary support for the language of the present claims.

16. Claims 144, 156-168, and 170-210 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection, as opposed to a "new matter" rejection. Accordingly, it is believed that the following are **new** grounds of rejection, *which have not been addressed, or considered by Applicant, the Office, or the Board of Patent Appeals and Interferences.*

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description'' Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereinafter, the "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

The claims are directed to a genus of antibodies that compete for binding to PSMA with a monoclonal antibody selected from the group consisting of E99, J415, J533, and J591 monoclonal antibody produced by hybridomas deposited under ATCC accession numbers HB-12101, HB-12109, HB12127, and HB-12126, respectively.

As explained in the above rejection of claims under 35 U.S.C. § 112, second paragraph, the claims are not necessarily limited to antibodies that completely abrogate

the interaction between any member of the recited pluralities of antibodies and PSMA, nor are the claims necessarily limited to antibodies that bind to the same antigenic determinant (i.e., epitope) of PSMA as any of the recited antibodies. To the contrary, when given the broadest, *reasonable* interpretation that is both consistent with the specification and that which would be understood by the skilled artisan, the claims are directed to any antibody or antigen-binding fragment thereof that inhibits or suppresses, at least to some measurable extent, binding of any member of the recited pluralities of antibodies to PSMA.

George et al. (cited *supra*) teaches that even antibodies that decidedly do not bind overlapping epitopes are able to compete to some measurable extent with other antibodies that bind the same antigen; and it is again submitted, as above, that any antibody, regardless of its antigenic binding specificity, is capable at high enough concentrations to at least partially inhibit binding of another antibody to an antigen recognized by that other antibody.

Accordingly, because the requisite degree to which the claimed antibody or antigen-binding fragment "competes" with any member of the recited pluralities of monoclonal antibodies for binding to PSMA is not specified by the claims, and is not ascertainable from the disclosure, the claims should be broadly interpreted to read on virtually any other antibody that binds PSMA, though not necessarily an antibody that binds the same, or even an overlapping epitope of PSMA, and not necessarily an antibody that competes for binding to PSMA to any particular extent, provided it competes to a measurable extent under some unspecified conditions.

As an additional comment regarding the breadth of the claims, although the disclosure might suggest the claims should *not* be interpreted as if directed to antibodies that do not bind PSMA, the claims themselves are not so limited, as they presently encompass any antibody or antigen-binding fragment thereof that competes for binding to PSMA with one of the recited monoclonal antibodies. As evidenced by George et al. (cited *supra*), for example, an antibody need not bind to the same, or even an overlapping epitope to exhibit some ability to "compete" for binding to an antigen with another antibody; if follows, especially at high enough concentrations, that any antibody,

regardless of its binding specificity, might under certain conditions compete for binding to an antigen with an antibody that binds that antigen. Accordingly, Applicant is reminded, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, while the specification merely describes antibodies that bind PSMA, the claims, which are not necessarily drawn to antibodies having such binding specificity, should perhaps be given their broader interpretation. If so, it is submitted that the specification does not provide written support for the claimed genus of antibodies or antigen binding fragments thereof, which include members that do not necessarily bind specifically to PSMA.

In contrast to the breadth of the claims, the specification describes with particularity only five different antibodies that bind PSMA: 7E11/CYT356, J591, J533, E99, and J415. The first of these antibodies is described by the prior art as binding the intracellular domain of PSMA, whereas the other antibodies (J591, J533, E99, and J415) are described in the specification as binding to the extracellular domain of the antigen. At paragraph [0106], for example, the specification discloses J591, J533, and E99 each interfered with binding of one another but did not block binding of J415, and vice versa; and 7E11/CYT356 did not block binding of any of J591, J533, E99, and J415.

Accordingly, the specification describes three antibodies that "compete" for binding to PSMA with one another, namely J591, J533, and E99; and it also describes two other antibodies (i.e., 7E11 and J415), which do not compete with any of the other antibodies that have been described.

Because each of monoclonal antibodies J591, J533, and E99 interferes with the others, the specification describes each as binding to the *same* epitope of PSMA; see, e.g., Example 10 at paragraphs [0104]-[0108] of the published application. Because none of monoclonal antibodies J591, J533, and E99 interferes with the binding of monoclonal antibodies 7E11/CYT356 or J415, the specification teaches these latter antibodies bind to *different* epitopes of PSMA.

It is submitted that there is inadequate description of the claimed genus of antibodies or antigen-binding fragments that compete for binding to PSMA with monoclonal antibody J415 to reasonably convey Applicant's possession of the claimed invention at the time the application was filed. Again, none of monoclonal antibodies J591, J533, E99, and 7E11/CYT356 are described as having the ability to "compete" for binding to PSMA with monoclonal antibody J415; moreover, no where in the specification is there literal support, much less any particular description of antibodies that compete for binding to PSMA with monoclonal antibody J415.

To the contrary, there may be in fact be implicit, if not explicit written support in the specification, as filed, for claims directed to a genus of antibodies or antigen-binding fragments thereof that bind PSMA, which compete for binding to PSMA with a monoclonal antibody selected from the group consisting of monoclonal antibodies J591, J533, and E99.

Nevertheless, although the present claims are not original claims, the "Guidelines" (cited *supra*) state, "the issue of a lack of written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant has possession of the claimed invention" (*Id.* at 1105). The "Guidelines" continue:

> The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.

The Federal Circuit has explained that *in ipsis verbis* support for the claims in the specification does not *per se* establish compliance with the written description requirement:

> Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *See also:* University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 1892 (CA FC 2004).

Thus, although the specification, as filed, may provide written support for the language of the claims, the disclosure must still be an adequate written description, *which establishes that the inventor was in possession of the invention.*

It is submitted that the disclosure would not reasonably convey to the skilled artisan that Applicant had possession of the claimed subject matter at the time the application was filed because it fails to adequately describe the genus of antibodies or antigen-binding fragments that bind specifically to PSMA and thereby "compete" for binding to the antigen with any one of the recited monoclonal antibodies.

It is further submitted that the claims, if indeed properly supported by the specification, as filed, should be *solely* directed to antibodies or antigen-binding fragments that bind to the *same* epitope as any of member of the recited pluralities of monoclonal antibodies (e.g., an E99 monoclonal antibody) and thereby compete for binding to PSMA with the particular member, or alternatively to antibodies or antigen-binding fragments that bind to a *different* epitope of PSMA and do not compete for binding to PSMA with the particular member. More pointedly, antibodies that "compete" for binding to PSMA with any of the recited monoclonal antibodies, which bind *overlapping* epitopes of PSMA, have not been described.

The specification insufficiently describes members of the genus of antibodies or antigen-binding fragments that bind antigenic determinants or epitopes of PSMA that are not recognized by any of monoclonal antibodies each of monoclonal antibodies J591, J533, and E99, which are able to compete with any of the latter for binding to PSMA. Again, although such antibodies or antigen-binding fragments thereof recognize epitopes that are distinct from those recognized by any of monoclonal antibodies each

of monoclonal antibodies J591, J533, and E99, as evidenced by George et al. (cited supra), for example, antibodies need not bind the same epitope, or even an overlapping epitope of an antigen to "compete" with another antibody for binding to the antigen. The specification does not describe particularly identifying structural and/or functional features, which would permit the skilled artisan to immediately envision, recognize, or distinguish at least a substantial number of the members of the claimed genus of antibodies or antigen binding fragments thereof, which bind to epitopes that differ from those recognized by monoclonal antibodies J591, J533, E99, or J415, or any other antibody to which the claims are directed. For example, the specification fails to describe the claimed genus in such a clear and particular manner to permit the skilled artisan to readily distinguish an antibody that binds to PSMA, *and* competes for binding to PSMA with monoclonal antibodies J591 or J415, from another antibody that also binds the antigen *but* does not compete with such a monoclonal antibody.

Furthermore, the specification insufficiently describes members of the genus of antibodies or antigen-binding fragments that bind the same antigenic determinants or epitopes of PSMA recognized by monoclonal antibodies J591, J533, and E99 and are accordingly able to compete with any of the latter for binding to PSMA. The specification fails to describe reliably predictable means for determining whether an antibody that binds PSMA binds to the same epitope of the antigen as any of monoclonal antibodies J591, J533, E99, or J415, or any other monoclonal antibody to which the claims are directed. As explained in greater detail below, the competition binding assay that has been exemplified cannot be used to establish with certainty whether two "competing" antibodies bind to the same epitope of an antigen; and furthermore, the conditions under which the assay is to be used to identify the claimed antibodies, which do or do not bind the same epitope, but which nevertheless "compete" with one of the recited monoclonal antibodies have not been described. For these reasons, the specification would not reasonably convey to one skilled in the art that Applicant had possession of the claimed invention at the time the application was filed.

Due to the unpredictable nature of the art, where the claimed antibodies are perhaps functionally related by their common abilities to "compete" with one of the

recited monoclonal antibodies, but unrelated structurally, absent sufficient description of the claimed invention, those that bind particular epitopes of PSMA cannot be envisioned, recognized or distinguished from other antibodies that also bind PSMA, albeit by the recognition of different epitopes. The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Where the claimed antibodies are functionally related as binding a common epitope of PSMA, whether the antibodies are or are not structurally related, the specification fails to describe the epitope to which the claimed antibodies bind. "[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes the genus of antibodies that bind any one particular epitope of PSMA, such as the epitope to which monoclonal antibody J591 binds, because no one particular epitope of PSMA to which such antibodies bind has been described. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Notably the Federal Circuit has recently decided that the description of a fully characterized molecular target of an antibody is sufficient to adequately describe an antibody that binds that target. See *Noelle v. Lederman*, 69 USPQ2d 1508 (CA FC 2004). However, the same court decided that each case involving the issue of written description, "must be decided on its own facts. Thus, the precedential value of cases in this area is extremely limited." *Vas-Cath*, 935 F.2d at 1562 (quoting *In re Driscoll*, 562 F.2d 1245, 1250 (C.C.P.A. 1977)).

In this instance, the claims are directed to a genus of antibodies that includes, but are not necessarily limited to antibodies that bind to PSMA, which, at least in structural terms, is generally considered a fully characterized antigen; however, the difference here is, although the antibodies bind PSMA, they only bind very particular

epitopes of PSMA that recognized by other monoclonal antibodies, such as monoclonal antibody J591, and are thereby able to "compete" with the latter for binding to PSMA. The specification describes these epitopes as residing in the extracellular domain of PSMA; see, e.g., paragraph [0029] of the published application. None of the epitopes to which any of the disclosed monoclonal antibodies binds have been described with the requisite degree of particularity however to permit the skilled artisan to recognize those epitopes.

Following the example set by the Federal Circuit in deciding *Noelle v. Lederman*, then, were the claims directed to an antibody that binds a well-characterized antigen, the written description would be met. However, the claims are not directed to an antibody that binds a well-characterized molecular target, but rather to an antibody that binds to *very discrete parts (i.e., epitopes) of PSMA*, which has not been characterized and remain cryptic in nature.

The term "epitope", as it is used in the art of immunology, is more generally used in a broader context to mean an "antigenic determinant", or site on the surface of an antigen molecule to which a single immunoglobulin molecule (e.g., antibody) binds; generally an antigen has several or many different antigenic determinants and reacts with antibodies of many different specificities. Stedman's Online Medical Dictionary, 27th Edition, which is available on the Internet at http://www.stedmans.com/, for example, defines the term "epitope' as "[t]he simplest form of an antigenic determinant, on a complex antigenic molecule, which can combine with antibody or T cell receptor".

Notably, Greenspan et al. (*Nature Biotechnology.* 1999; **7**: 936-937), for example, teaches that defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include any and all residues that make contact with a ligand, here an antibody; even contacts by residues that are energetically neutral, or even destablilizing to binding are constitutive. Greenspan et al. teaches an epitope will not include any residue not contacted by the ligand (i.e., an antibody), even though substitution of such a residue by another might

profoundly affect binding. Accordingly, it follows the epitope to which any given ligand binds can only be identified empirically.

Thus, even using a competition binding assay, such as that described in Example 10 of the specification, the skilled artisan cannot recognize or distinguish an antibody that binds the same epitope as another antibody because antibodies that compete with one another for binding to the same antigen do not necessarily bind the same epitope; rather, an antibody may bind a spatially overlapping epitope and thereby sterically hinder binding of the other ligand to its epitope, or as evidenced by George et al. (cited *supra*), an antibody may bind an epitope that is distant from, and spatially non-overlapping with the epitope of an antigen recognized by the other antibody, and still interfere with binding of the latter to the antigen.

Where the claimed antibodies bind an epitope of PSMA recognized by any of the recited monoclonal antibodies, it is aptly noted that the Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability to bind a particular epitope of PSMA, or the ability to "compete" for binding to PSMA with any of the recited monoclonal antibodies, does not provide an adequate written description of the genus. See *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Although *Lilly* related to claims drawn to genetic material, the statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to

distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1984 (CAFC 2004). Without the antibodies to which the claims are directed, it is impossible to make or use the claimed invention.

In addition, although the skilled artisan could initially screen candidate antibodies to identify those that are possibly encompassed by the claims by performing, for example, a competitive binding assay, and then empirically determine whether the selected antibodies bind to the same epitope recognized by one of the recited monoclonal antibodies, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating (or identifying) it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

"Guidelines" (cited *supra*) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of antibodies, which vary both structurally and functionally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show

that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

17. Claims 144, 156-168, and 170-210 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** a monoclonal antibody selected from the group consisting of J591, J533, E99, and J415 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively, an antigen-binding fragment thereof, a composition comprising said antibody or antigen-binding fragment, a kit for detecting prostate cancer comprising said antibody or antigen-binding fragment, and a hybridoma selected from the group consisting of the hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, **and while being enabling for making and using** an antibody or antigen binding fragment thereof described by the prior art, which is encompassed by the claims, a composition or kit comprising such an antibody or antigen binding fragment described by the prior art, as well as a hybridoma or other cell line producing such an antibody, **does not reasonably provide enablement for making and/or using** any antibody or antigen-binding fragment that competes with a monoclonal antibody selected from the group consisting of E99, J415, J533 and J591 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively, for binding to PSMA, yet does not necessarily specifically bind to PSMA, an composition thereof, a kit for detecting any type of cancer comprising such an antibody or antigen-binding fragment thereof, or a cell that produces such an antibody. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and./or unreasonable experimentation.

As explained in the rejections above (e.g., the rejection of claims under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement), the claims are directed to a genus of antibodies or antigen-binding fragments thereof, which do not necessarily bind PSMA, or more particularly do not necessarily bind to the same epitope as any of monoclonal antibodies J591, J533, E99, and J415 produced by

hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109. Rather, because as evidenced by George et al. (cited *supra*), for example, an antibody need not bind the same epitope of an antigen to "compete" for binding to that antigen with another antibody, the claims should broadly, but reasonably be interpreted to encompass any antibody, not necessarily an antibody that binds to the same epitope as any of monoclonal antibodies J591, J533, E99, and J415, and perhaps not necessarily an antibody that binds to PSMA.

Yet, the specification would only reasonably enable use of an antibody that specifically binds to PSMA, as opposed to any antibody that is capable of competing for binding to PSMA with one of the recited antibodies, yet does not specifically bind to PSMA.

Furthermore, the claimed antibodies or antigen binding fragments thereof, which compete for binding to PSMA with any of a plurality of recited monoclonal antibodies, include but are not limited to antibodies or antigen-binding fragments that bind to the same or a different epitope as a member of any of the recited monoclonal antibodies; see, e.g., paragraph [0104] of the published application. As explained above, the specification describes monoclonal antibodies J591, J533, and E99 as each capable of interfering with binding of the others to PSMA but incapable of competing for binding to PSMA with monoclonal antibodies J415 and 7E11/CYT356, and vice versa. Because each of monoclonal antibodies J591, J533, and E99 interferes with the others, the specification teaches each binds to the same epitope of PSMA; and because none of monoclonal antibodies J591, J533, and E99 interfere with the binding of monoclonal antibodies J415 and 7E11/CYT356, and vice versa, the specification teaches the latter antibodies bind different epitopes.

However, as also explained above in the rejections of claims under 35 U.S.C. § 112, first and second paragraphs, the claims do not define the extent to which the claimed antibody or antigen binding fragment "competes", nor do they define the methodology by which such a determination is made, and under what conditions. As evidenced by George et al. (cited supra), for example, at a high enough concentration, or under certain conditions, *any* antibody is expected to "compete" for binding to the

antigen with the other antibody; though perhaps another antibody that binds the same antigen, or more particularly the same epitope of an antigen or an overlapping epitope recognized by a given antibody would be expected to more effectively compete than an antibody that binds to some other antigen or a distinct portion of the same antigen.

So, therefore, even were the claims limited to antibodies that specifically bind to PSMA and compete for binding to PSMA with any one of the recited monoclonal antibodies, for the reasons set forth in the above rejection, an antibody that competes for binding does not necessarily bind to the same epitope an another antibody. Rather, an antibody may bind a spatially overlapping, but distinct epitope of PSMA, and still compete for binding to PSMA with one of the recited monoclonal antibodies.

This is because antibodies that bind overlapping epitopes of the same antigen act to sterically inhibit binding of others, even though each recognizes a discrete epitope of the antigen; so, a competition-binding assay can thus not serve to identify antibodies that bind the same epitope.

Accordingly, to whatever extent the claims are drawn to an antibody or antigen binding fragment that binds to the same epitope as any one of the recited monoclonal antibodies, so as to be capable of competing with the latter for binding to PSMA, it is submitted that it would not be a merely routine matter to make the claimed antibody that is capable of binding to the same epitope as monoclonal antibody J415, for example, which is accordingly capable of competing for binding to PSMA with the monoclonal antibody. As evidenced by the teachings of Greenspan (cited supra), for example, the skilled artisan cannot readily determine if an antibody binds to the same epitope as another antibody without first determining the epitopes to which both antibodies bind. Moreover, Greenspan teaches the determination and characterization of the epitope to which an antibody binds is not routine or conventional and would require undue and unreasonable experimentation.

One could potentially eliminate some antibodies that bind discrete epitopes of PSMA, which are distinct from that to which any of the recited monoclonal antibodies bind, such as monoclonal antibody J591, because, depending upon the conditions under which the assay is performed, these antibodies might not compete as effectively

as others for binding to PSMA. However, it is not possible to identify using such competition binding assays antibodies that bind to the *same epitope* of an antigen. Again, the epitope to which any antibody binds can only be determined empirically using very complex methodology, such as crystallography, mutagenesis, and/or very sensitive binding assays, and arduous analyses of the resulting data.

Therefore, because the artisan cannot predict whether two competing antibodies bind to the same epitope, or different but overlapping epitopes, the epitope binding specificity of an antibody can only be determined empirically. As such, to any extent that the claims are directed to an antibody or antigen binding fragment thereof that binds to the same epitope as any of monoclonal antibodies J591, J533, E99, and J415 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively, the specification would not provide sufficiently enabling disclosure of the claimed invention, which could only be made, and then used, by performing undue and/or unreasonable experimentation.

Although the prior art enables one to make and use many antibodies, which under certain conditions, could demonstrably "compete" for binding to PSMA with any of monoclonal antibodies J591, J533, E99, and J415 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, Applicant is reminded that to satisfy the enablement requirement, reasonable correlation must exist between the scope of the claims and scope of enablement set forth in the specification. Furthermore, although a specification need not, and preferably omits teachings well known in the prior art, in deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997). Thus, the overly broad scope of the claims would merely serve as an invitation to one skilled in the art to identify antibodies and

antigen-binding fragments thereof, which under certain, albeit unspecified assay conditions "compete" for binding to PSMA with any member of the recited pluralities of monoclonal antibodies; yet, defining a substance by its principal biological activity amounts to an alleged conception having no more specificity than that of a wish to know the identity of any material with that biological property. See *Colbert v. Lofdahl*, 21 USPQ2d 1068, 1071 (BPAI 1991).

Therefore, in conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

19. Claims 144, 156-161, 164, 171-173, and 178-210 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,962,981 B1, as evidenced by Liu et al. (*Cancer Res.* 1998 Sep 15; **58**: 4055-4060) and George et al. (*Circulation.* 1998; **97**: 900-906).

Here, the rejected claims are directed to an antibody or antigen binding fragment thereof that competes for binding to PSMA with a monoclonal antibody selected from the group consisting of E99, J415, J533, and J591 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively.

U.S. Patent No. 6,962,981 B1 (Murphy et al.) teaches monoclonal antibodies and antigen binding fragments thereof that bind specifically to the extracellular domain of PSMA; see entire document (e.g., the abstract; Figure 20; column 27, Table 2). Murphy et al. teaches hybridomas producing the disclosed monoclonal antibodies; see, e.g., columns 29 and 30. Murphy et al. teaches the fragments of the disclosed monoclonal antibodies are Fab fragments, F(ab')2) fragments, and Fv fragments; see, e.g., column 14, lines 8-17. Murphy et al. teaches the disclosed monoclonal antibodies or antigen binding fragments thereof are conjugated (bound) to a cytotoxic drug, namely radioisotopes, chemotherapeutic drugs, and toxins; see, e.g., column 14, lines 37-52. Murphy et al. teaches the antibodies or antigen binding fragments thereof are conjugated to beta-emitters (i.e., positron emitting isotopes); see, e.g., column 14, lines 25-36. Murphy et al. teaches the antibodies or antigen binding fragments thereof are conjugated to streptavidin[2] and other biological proteins, which are used as therapeutic agents; see, e.g., column 15, lines 10-30. Murphy et al. teaches the antibodies or antigen binding fragments thereof are labeled with any of a variety of "reporter" substances, including, for example, radioactive isotopes and fluorogenic compounds; see, e.g., column 14, lines 26-36. Murphy et al. teaches isolated clones producing the disclosed antibodies, which are derived from primary hybridomas (i.e., "lymphocytic[3] cell

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[2] Notably, streptavidin is a biological protein of bacterial origin. Murphy et al. teaches antibodies conjugated to streptavidin and bound to a biotinylated cytotoxin are used therapeutically; see, e.g., column 15, lines 26-30.

[3] The term "lymphocytic" is defined by The On-line Medical Dictionary (available on the Internet at http://cancerweb.ncl.ac.uk/omd/), for example, as meaning: "Pertaining to, characterised by or of the nature of lymphocytes" (© Copyright1997-2005 - The CancerWEB Project). The hybridomas disclosed by Murphy et al. are fusions of B lymphocytes and myeloma cell lines (see, e.g., column 7, line 13, through column 8, line 65. Accordingly, the disclosed clones producing the disclosed monoclonal antibodies, which were derived from primary hybridomas, are deemed the same as the claimed cells derived from "lymphocytic cell lines".

lines"); see, e.g., column 21, lines 35-65. Murphy et al. teaches compositions comprising the antibodies or antigen binding fragments thereof, which are suitably used in a variety of applications, including immunohistological and immunocytochemical applications, and diagnostic and therapeutic applications; see, e.g., column 11, line 26, through column 15, line 30. Accordingly, such compositions, particularly those used in therapeutic compositions, are necessarily further comprised of pharmaceutically acceptable carriers, excipients, and/or stabilizers. Murphy et al. teaches kits for use, for example, in diagnosing prostate cancer, which comprise such compositions comprising the disclosed antibodies or antigen binding fragments thereof; see, e.g., column 15, lines 31-43.

Although Murphy et al. does not expressly teach any of the disclosed antibodies or antigen binding fragments thereof "compete" for binding to PSMA with monoclonal antibodies J591, J415, J533, and/or E99, because the disclosed antibodies bind the extracellular domain of PSMA, there is a reasonable presumption that the antibodies do so. As evidenced by George et al. (cited *supra*), an antibody need not bind to the same epitope of an antigen as another antibody to measurably "compete" for binding to the antigen with the other antibody. Thus, at a high enough concentration, or under certain conditions, *any* antibody, but perhaps especially another antibody that binds the same antigen, or more particularly the same epitope recognized by another antibody or an overlapping epitope of the antigen, is expected to "compete" for binding to the antigen with the other antibody. As thoroughly explained above in the rejections of claims under 35 U.S.C. § 112, first and second paragraphs, the claims do not define the extent to which the claimed antibody or antigen binding fragment "competes", nor do they define the methodology by which such a determination is made, and under what conditions. Therefore, absent a showing of any difference, the antibodies and antigen binding fragments disclosed by Murphy et al. are deemed the same as the claimed antibodies and antigen binding fragments thereof.

Notably, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional

characteristics as the antibodies and antigen binding fragments thereof. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the antibodies and antigen binding fragments thereof are different than those taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

Furthermore, although Murphy et al. does not expressly teach any of the disclosed antibodies is internalized with PSMA, as evidenced by Liu et al., each of monoclonal antibodies J591, J415, J533, and E99 are internalized with PSMA by LNCaP cells (see entire document; e.g., page 4056, column 1). Accordingly, there is a reasonable presumption that the antibodies disclosed by Murphy et al., which bind to the extracellular domain of PSMA, are internalized with the antigen, particularly since the disclosed antibodies bind the same antigen.

20. Claims 144, 156-158, 172, 173, 178, 180, 186, 187, 194, and 195 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al. (Cancer Res. 1997 Sep 1; **57**: 3629-3634) (of record; cited by Applicant), as evidenced by Liu et al. (*Cancer Res.* 1998 Sep 15; **58**: 4055-4060) (of record; cited by Applicant).

Here, the rejected claims are directed to an antibody that competes for binding to PSMA with a monoclonal antibody selected from the group consisting of E99, J415, J533, and J591 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively.

Liu et al. teaches monoclonal antibodies 7E11, J591, J533, J415, and E99; see entire document (e.g., page 3631, Figure 3). Liu et al. teaches the antibodies bind to PSMA; monoclonal antibody 7E11 binds the intracellular domain, whereas monoclonal antibodies J591, J533, J415, and E99 bind the extracellular domain (see, e.g., the abstract). Liu et al. teaches hybridomas producing the disclosed monoclonal antibodies; see, e.g., page 3629, column 2. Liu et al. teaches compositions comprising the disclosed antibodies and, absent a showing otherwise, pharmaceutically acceptable carriers or excipients; see, e.g., page 3629, column 1, through page 3631, column 1. Liu et al. teaches each of monoclonal antibodies J591, J533, and E99 "competed" for

binding to PSMA with any of the others; see, e.g., column 3632, column 2. Liu et al. teaches monoclonal antibody J415 competed only with itself; see column 3632, column 2. Liu et al. teaches the disclosed antibodies are bound by a label (i.e., bound to a fluorescently labeled secondary antibody); see, e.g., page 3630, column 2; and page 3631, Figure 3. Liu et al. teaches the antibodies are bound by other detectable labels (i.e., peroxidase- and gold-conjugated secondary antibodies); see, e.g., page 3629, column 1; and page 3630, column 2). Liu et al. teaches the antibodies were labeled by biotinylation, which enabled their detection and quantification; see, e.g., page 3630, column 2; and page 3633, Figure 5.

Although Liu et al. does not expressly teach any of the disclosed antibodies is internalized with PSMA, as evidenced by Liu et al. (1998), each of monoclonal antibodies J591, J415, J533, and E99 are internalized with PSMA by LNCaP cells (see entire document; e.g., page 4056, column 1).

21. Claims 144, 156, 158, 172, 173, 180, 186, 187, 194, and 195 are rejected under 35 U.S.C. 102(b) as being anticipated by Israeli et al. (*Cancer Res.* 1994 Apr 1; **54** (7): 1807-1811) (of record; cited by Applicant), as evidenced by George et al. (*Circulation.* 1998; **97**: 900-906).

Here, the rejected claims are directed to an antibody that competes for binding to PSMA with a monoclonal antibody selected from the group consisting of E99, J415, J533, and J591 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively.

Israeli et al. teaches monoclonal antibody 7E11; see entire document (e.g., abstract). Israeli et al. teaches the antibody bind to PSMA; see, e.g., the abstract. Israeli et al. teaches compositions comprising the disclosed antibody and, absent a showing otherwise, pharmaceutically acceptable carriers or excipients, such as, e.g., a buffered saline solution; see, e.g., page 1807, column 2, through page 1808, column 1. Liu et al. teaches the disclosed antibody is bound by a label (i.e., bound to a radioactively labeled secondary antibody); see, e.g., page 1808, column 1; and page 1809, Figure 3.

Although Israeli et al. does not expressly teach the disclosed antibody "competes" for binding to PSMA with monoclonal antibodies J591, J415, J533, and/or E99, as evidenced by George et al. (cited *supra*), an antibody need not bind to the same epitope of an antigen as another antibody to measurably "compete" for binding to the antigen with the other antibody. Thus, at a high enough concentration, or under certain conditions, *any* antibody, including an antibody that binds to a different epitope of an antigen than the epitope recognized by another antibody that binds the antigen is expected to "compete" for binding to the antigen with the other antibody. Furthermore, although the specification teaches the antibody disclosed by Israeli et al. (monoclonal antibody 7E11) does not "compete" for binding to PSMA with any of monoclonal antibodies J591, J415, J533, and E99, neither the claims nor the disclosure delineate the conditions under which such a determination was made. Moreover, as thoroughly explained above in the rejections of claims under 35 U.S.C. § 112, first and second paragraphs, the claims do not define the extent to which the claimed antibody or antigen binding fragment "competes", nor do they define the methodology by which such a determination is made, and under what conditions. Nevertheless, under certain conditions, monoclonal antibody 7E11 is expected to "compete" to some measurable extent for binding to PSMA with monoclonal antibodies J591, J415, J533, and/or E99. Therefore, absent a showing of any difference, the antibody disclosed by Israeli et al. is deemed the same as the claimed antibodies and antigen binding fragments thereof.

Again, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the antibodies and antigen binding fragments thereof. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the antibody disclosed by the prior art differs from the claimed antibody.

22. Claims 144, 156-161, 167, 170-173, 177, 178, 180, 184-203, 209,and 210 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,538,866 A, as evidenced by George et al. (*Circulation*. 1998; **97**: 900-906).

Here, the rejected claims are directed to a polyclonal or monoclonal antibody, which competes for binding to PSMA with a monoclonal antibody selected from the group consisting of E99, J415, J533, and J591 produced by hybridomas deposited under ATCC deposit accession numbers HB-12126, HB-12127, HB-12101, and HB-12109, respectively.

U.S. Patent No. 5,538,866 A (Israeli et al.) teaches polyclonal and monoclonal antibodies that bind specifically to PSMA; see entire document (e.g., column 6, lines 44-47). Israeli et al. teaches the antibody binds the extracellular domain of the antigen, so as to be capable of binding to the surface of prostate cancer cells expressing the antigen; see, e.g., column 13, lines 10-18. Israeli et al. teaches the antibody is conjugated to a cytotoxic drug, namely a radioisotope or biological toxin, such as endotoxin or ricin, which are proteins of bacterial and plant origins, respectively; see, e.g., column 13, lines 5-9; and column 23, lines 44-52. Notably, radioisotopes are detectable labels. Israeli et al. teaches the antibody is conjugated to $Indium^{111}$, a gamma ray emitter; see, e.g., column 13, lines 17 and 18. Israeli et al. teaches a composition comprising the antibody and a pharmaceutically acceptable carrier, excipient, or stabilizer; see, e.g., column 13, lines 22-24. Israeli et al. teaches hybridomas producing the disclosed antibodies; see, e.g., column 12, lines 55-60.

Although Israeli et al. does not expressly teach the disclosed antibody "competes" for binding to PSMA with monoclonal antibodies J591, J415, J533, and/or E99, as evidenced by George et al. (cited *supra*), an antibody need not bind to the same epitope of an antigen as another antibody to measurably "compete" for binding to the antigen with the other antibody. Thus, at a high enough concentration, or under certain conditions, *any* antibody, including an antibody that binds to a different epitope of an antigen than the epitope recognized by another antibody that binds the antigen is expected to "compete" for binding to the antigen with the other antibody. Neither the claims nor the disclosure delineate the conditions under which such a determination was made. Moreover, as thoroughly explained above in the rejections of claims under 35 U.S.C. § 112, first and second paragraphs, the claims do not define the extent to which the claimed antibody or antigen binding fragment "competes", nor do they define

the methodology by which such a determination is made, and under what conditions. Nevertheless, the antibodies disclosed by the prior art are polyclonal; polyclonal antibodies raised against PSMA bind a plurality of epitopes of PSMA, and are reasonably expected to comprise one or more species of antibody that bind to the same epitopes as monoclonal antibodies J591, J415, J533, and/or E99 and thereby "compete" for binding to PSMA with one or more of the monoclonal antibodies. In addition, because the disclosed antibodies bind the extracellular domain of PSMA, there is a reasonable presumption that the disclosed monoclonal antibodies also "compete" for binding to PSMA with one or more of the recited monoclonal antibodies, especially since, under certain conditions, any monoclonal antibody that binds to PSMA is expected to "compete" to some measurable extent for binding to PSMA with one or more of those antibodies. Therefore, absent a showing of any difference, the polyclonal or monoclonal antibodies disclosed by Israeli et al. are deemed the same as the claimed antibodies and antigen binding fragments thereof.

Again, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the antibodies and antigen binding fragments thereof. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the antibody disclosed by the prior art differs from the claimed antibody.

23. Claims 144, 156-168, and 170-210 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication No. 2004/0213791 A1 or U.S. Patent Application Publication No. 2004/0120958 A1.

U.S. Patent Application Publication No. 2004/0213791 A1 (Bander et al.) teaches anti-PSMA antibodies or antigen binding fragments thereof, wherein said antibodies comprise the complementarity determining regions (CDRs) of any of monoclonal antibodies J591, J415, J533 and E99, or hybridomas, or other cell lines producing such antibodies; see entire document (e.g., the abstract; the claims; paragraph [0012]). These antibodies bind to the same epitope(s) as monoclonal antibodies J591, J415,

J533 and/or E99 and therefore "compete" for binding to PSMA with any one or more of those monoclonal antibodies.

Furthermore, at paragraph [0014] Bander et al. teaches the anti-PSMA antibody binds all or part of an epitope bound by an antibody described herein, e.g., a J591, E99, J415, and J533 antibody. Bander et al. teaches the anti-PSMA antibody can inhibit, e.g., competitively inhibit, the binding of an antibody described herein, e.g., a J591, E99, J415, and J533 antibody, to human PSMA; and Bander et al. teaches an anti-PSMA antibody may bind to an epitope, e.g., a conformational or a linear epitope, which epitope when bound prevents binding of an antibody described herein, e.g., a J591, E99, J415, and J533 antibody. Bander et al. teaches the epitope can be in close proximity spatially or functionally-associated, e.g., an overlapping or adjacent epitope in linear sequence or conformational space, to the one recognized by the J591, E99, J415, or J533 antibody.

Bander et al. teaches fragments of such antibodies are selected from the group consisting of Fab, $F(ab')_2$, Fv, and single chain Fv fragments; see, e.g., paragraph [0017]. Bander et al. teaches the antibodies or antigen binding fragments are internalized with PSMA; see, e.g., paragraph [0199]. Bander et al. teaches the antibodies or antigen binding fragments thereof are coupled to a cytotoxic moiety selected from a cytotoxic protein of plant, fungal, or bacterial origin, a radioisotope that emits alpha, beta, or gamma radiation, a cytotoxic or therapeutic drug (e.g., a taxane); see, e.g., paragraphs [0145] and [0390]. Bander et al. teaches the antibodies or antigen binding fragments thereof, which are coupled to a label selected from biologically active enzymes, prosthetic groups, luminescent materials, bioluminescent materials, fluorescent materials, paramagnetic materials and radioactive ions; see, e.g., paragraph [0145]. Bander et al. teaches the radioisotopes to which the claimed antibodies or antigen binding fragments are coupled are selected from ^{212}Bi, ^{213}Bi, ^{211}At, ^{186}Re, ^{90}Y, ^{131}I, ^{32}P, ^{125}I, ^{3}H, ^{14}C, ^{188}Rh, and ^{99}mTc; see, e.g., paragraph [0391]. Bander et al. teaches pharmaceutical compositions comprising the antibodies or antigen binding fragments thereof and a pharmaceutically acceptable carrier, excipient, or stabilizer; see, e.g., paragraph [0147]. Bander et al. teaches kits comprising the disclosed

antibodies and antigen binding fragments thereof; see, e.g., paragraphs [0367]-[0371]. Bander et al. teaches the cells producing the antibodies are derived from lymphocytic cell lines; see, e.g., paragraph [0349].

U.S. Patent Application Publication No. 2004/0120958 A1 is a continuation-in-part of the earlier filed application, namely copending Application No. 10/379,838, which is a continuation-in-part of another earlier filed application, which was published as the above cited U.S. Patent Application Publication No. 2004/0213791 A1. Accordingly, absent a showing otherwise, it is submitted that U.S. Patent Application Publication No. 2004/0120958 A1 teaches the subject matter taught by U.S. Patent Application Publication No. 2004/0213791 A, which has been incorporated in its entirety by reference therein, and therefore provides a disclosure that anticipates the inventions of claims 144, 156-168, and 170-210.

24. Claims 144, 156-168, and 170-210 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 10/379,838 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if published under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future publication or patenting of the copending application.

Notably, copending Application No. 10/379,838 has not been published.

Copending Application No. 10/379,838 is a continuation-in-part of the earlier filed application published as the U.S. Patent Application Publication No. 2004/0213791 A1, which is cited as the basis of the rejection set forth in section 17 above. Accordingly, absent a showing otherwise, it is submitted that the specification of copending Application No. 10/379,838 teaches the subject matter taught by U.S. Patent Application Publication No. 2004/0213791 A, which has been incorporated in its entirety by reference therein, and therefore provides a disclosure that anticipates the inventions of claims 144, 156-168, and 170-210.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Response to Amendment

25. The declaration under 37 C.F.R. § 1.132 filed May 2, 2005, is insufficient to overcome the *instant* rejection of claims 144, 156-168, and 170-210 under 35 U.S.C. § 112, first paragraph, which is based upon the insufficiency of the disclosure as set forth in *this* Office action for the following reasons:

Again, as explained above, the instant rejection of the claims under 35 U.S.C. §112, first paragraph, as failing to satisfy the written description requirement, it is believed an issue that *has thus far not been addressed, or considered by Applicant, the Office, or the Board of Patent Appeals and Interferences.*

The declaration by Abbie Cerlinker, Ph.D., states one ordinarily skilled in the art at the time the application was filed would have understood that the specification, as originally filed, provides written support for the language of the claims, which are drawn to antibodies or antigen binding fragments thereof that compete for binding to PSMA with a monoclonal antibody selected from the group consisting of a E99, a J415, a J533, and a J591 monoclonal antibody. In particular, the declaration cites the specification at page 27, line 26, through page 28, line 6, as providing explicit support for the present claims, which, at section 8 of the declaration, Dr. Cerlinker opines would have shown actual possession of the subject matter encompassed by those claims.

The merit of the declaration by Dr. Cerlinker has been carefully considered but not found sufficient to overcome the grounds of rejection of claims 144, 156-168, and 170-210 under 35 U.S.C. § 112, first paragraph, as a disclosure that describes the claimed subject matter with the requisite degree of particularity to reasonably convey to one skilled in the relevant art that, at the time the application was filed, Applicant had

possession of the claimed invention. As explained in the "written description" rejection set forth in section 10 above, although the specification, as filed, may indeed provide written support for the language of the claims, the disclosure must still be an adequate written description, *which establishes that the inventor was in possession of the invention*. Contrary to Dr. Cerlinker's opinion, it is submitted that the disclosure would not reasonably convey to the skilled artisan that Applicant had possession of the claimed subject matter at the time the application was filed because it fails to adequately describe the genus of antibodies or antigen-binding fragments that bind specifically to PSMA and thereby "compete" for binding to the antigen with any one of the recited monoclonal antibodies. Applicant is referred to section 10 above for a discussion of the particular reasons the disclosure is considered insufficiently descriptive of the claimed subject matter to satisfy the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

Conclusion

26. No claim is allowed.

27. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. U.S. Patent No. 6,150,508 A (of record; cited by Applicant) teaches monoclonal antibodies and antigen binding fragments thereof that bind specifically to the extracellular domain of PSMA. Murphy et al. (*Prostate*. 1996 Apr; **28** (4): 266-271) (of record; cited by Applicant) teaches anti-PSMA monoclonal antibodies 7E11 and 3F5.4G6, the latter of which binds the extracellular domain of the antigen. Horoszewicz et al. (*Anticancer Res.* 1987 Sep-Oct; **7** (5B): 927-935) (of record; cited by Applicant) teaches anti-PSMA monoclonal antibody 7E11.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stephen L. Rawlings, Ph.D.
Primary Examiner
Art Unit 1643

slr
March 28, 2007